Registration Decision for the New Active Ingredient Flupyradifurone

Approved by: _____

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Summary

This document announces that the U.S. Environmental Protection Agency (EPA) has completed its evaluation of the new insecticide flupyradifurone and has concluded that it meets the regulatory standard under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). Two products will be registered under Section 3(c)(5) of FIFRA, the technical formulation "Flupyradifurone TC," and an end-use formulation "Sivanto™ 200 SL."

Flupyradifurone is classified as a Reduced Risk pesticide. In comparison to the registered alternatives, flupyradifurone presents a less hazardous ecological and human health profile. The alternatives include neonicontinoids, organophosphates and pyrethroids. Registration of flupyradifurone will provide many growers of very diverse crops across the U.S. with a new pest management tool that presents an effective countermeasure to resistance development.

Background

On October 30, 2012, EPA received an application from Bayer Crop Science for registration of the new insecticide flupyradifurone (CAS Number 951659-40-8), which will be sold under the trade name "Sivanto." The application was also submitted for simultaneous review by the Pest Management Regulatory Agency (PMRA) of Canada and the Australian Pesticides and Veterinary Medicines Authority (APVMA). The EPA, the PMRA and the APVMA combined their resources in terms of scientific and regulatory expertise and conducted a "joint review" of flupyradifurone. Each country led the initial (primary) review of particular elements of the overall data package containing a total of 437 studies; EPA was the primary reviewer of the metabolism studies and North American field trials; PMRA was the lead reviewer of the product chemistry, environmental fate and the ecological toxicity studies. Canada also split the primary review of the mammalian acute toxicity studies with the APVMA. The APVMA was the lead reviewer for the mammalian chronic toxicity studies which in combination with the acute mammalian studies are used to evaluate potential effects on human health. Each country's team of scientists peer-reviewed the primary reviews of their counterparts to reach consensus on the evaluation of the data. While continuing to consult and coordinate, human health and ecological risk assessments were developed by each country individually.

Pesticides can be classified according to their mode of action (MoA) and their structure. One classification scheme is that developed by the Insecticide Resistance Action Committee (IRAC) to assist growers and crop protection professionals in selecting pesticides that can be used in an effective insecticide resistance management strategy. Under the IRAC classification process, flupyradifurone falls within a group of pesticides that inhibit the nicotinic acetylcholine receptor (IRAC Group 4). Similar to other neurotoxic chemicals that inhibit acetylcholine receptors (*e.g.* Group 1), there are multiple sub-groups within each group where chemicals are further sorted by differences in their chemical structure, receptor binding properties, and susceptibility to degradation. For example in Group 1, there are two subgroups, *i.e*, Subgroups 1A (carbamates) and 1B (organophosphates) that have distinctly different properties but both inhibit acetylcholinesterase enzyme activity. Within IRAC Group 4, there are four subgroups of chemicals, *i.e*., Subgroups 4A (neonicotinoids), 4B (nicotine), 4C (sulfoxaflor) and 4D (butenolides), grouped as agonists of the nicotinic acetylcholine receptor. Flupyradifurone is

classified as a "butenolide" insecticide (IRAC group 4D) and while it targets the nicotinic acetylcholine receptor, it differs from other chemicals within Group 4 in terms of how it binds to the receptor and the extent to which it is metabolized. The differences between flupyradifurone and members of the other three subgroups provide advantages to the new subgroup (butenolides) that are useful in terms of insect resistance management.

Flupyradifurone is intended to be taken up and distributed to various parts of the plant (*i.e.*, the chemical is systemic) to protect against piercing and sucking insects such as aphids, whiteflies, thrips, and psyllids, all of which have become increasingly resistant to other classes of insecticides and are difficult to control. It was proposed to be registered as a liquid formulation applied by foliar application, chemigation and/or soil drench to the following crops:

- Bushberry, Except Cranberry (Crop Subgroup 13-07B);
- Low Growing Berry Except Cranberry (Crop Subgroup 13-07G);
- Bulb Vegetables (Crop Group 3-07);
- Cereal Grains Except Rice (Crop Group 15);
- Citrus Fruits (Crop Group 10-10);
- Cottonseed (Crop Subgroup 20C);
- Cucurbit Vegetables (Crop Group 9);
- Edible Podded Legume Vegetables (Crop Subgroup 6A);
- Succulent Shelled Pea and Bean (Crop Subgroup 6B);
- Dried Shelled Pea and Bean (except Soybean);
- Foliage of Legume Vegetables (except Soybean) (Crop Subgroup 7A);
- Non-grass Animal Feeds (Alfalfa and Clover only);
- Forage, Fodder, and Straw of Cereal Grains (Crop Group 16);
- Fruiting Vegetables (Crop Group 8-10);
- Hops;
- Head and Stem Brassica Vegetables (Crop Subgroup 5A);
- Leafy Brassica Greens (Crop Subgroup 5B);
- Leafy Vegetables (Except Brassica) (Crop Group 4);
- Peanuts;
- Pitaya;
- Pome Fruits (Crop Group 11-10);
- Prickly Pear Cactus; Root Vegetables Except Sugar Beet (Crop Subgroup 1B);
- Small Fruit Vine Climbing (Except Fuzzy Kiwifruit) (Crop Subgroup 13-07F);
- Taro Leaves;
- Tree nuts (Crop Group 14-12);
- Turnip Greens; and Tuberous
- Corm Vegetables (Crop Subgroup 1C).

Flupyradifurone was also proposed for registration as a seed treatment for soybeans. There were no residential use sites proposed.

Evaluation

In evaluating a pesticide registration application, the EPA assesses a wide variety of exposure information (i.e., where and how the pesticide is used) and environmental fate (*i.e.*, how the chemical will move in the environment) and toxicity studies (*i.e.*, effects on humans and other non-target organisms) to determine the likelihood of adverse effects (*i.e.*, risk) from exposures associated with the proposed use of the product. Risk assessments are developed to evaluate the environmental fate of the compound as well as how it might affect a wide range of non-target organisms including humans, terrestrial and aquatic wildlife (plants and animals). On the basis of these assessments, EPA evaluates and approves language for each pesticide label to ensure the directions for use and safety measures are appropriate to mitigate any potential risk. In this way, the pesticide's label helps to communicate essential limitations and mitigations that are necessary for public safety. It is a FIFRA violation to use a pesticide in a way that conflicts with the label.

1. Assessment of Risk to Human Health

EPA requires a wide range of studies in order to assess a pesticide. For flupyradifurone, the database of studies required to support the assessment of risk to human health is complete.

The acute toxicity of flupyradifurone was low for all routes of exposure (oral, dermal, and inhalation). Table 1 summarizes the toxicological endpoints used in the human health risk assessment. The acute endpoint is based on the clinical signs of neurotoxicity in the acute neurotoxicity study in rats. The chronic, short- and intermediate-term endpoint is based on the skeletal muscle myofiber atrophy/degeneration from the 1-year oral toxicity study in dogs.

Table 1.--Summary of Toxicological Doses and Endpoints for flupyradifurone, for Use in Human Health Risk Assessment

Exposure/Scenario	Point of Departure and Uncertainty/Safety Factors	RfD, PAD, LOC for Risk Assessment	Study and Toxicological Effects
Acute dietary (All populations)	NOAEL = 35 mg/kg/day UF_A = 10x UF_H = 10x FQPA SF = 1x	Acute RfD = .35 mg/kg/day	**Acute neurotoxicity study – rat** LOAEL = 50 mg/kg/day
Chronic dietary (All populations)	NOAEL= 7.8 mg/kg/day UF_A = 10x UF_H = 10x FQPA SF = 1x	Chronic RfD = .078 mg/kg/day cPAD = .078 mg/kg/day	**1-year oral toxicity study-dog** LOAEL= 28 mg/kg/day
Cancer (Oral, dermal, inhalation)	Flupyradifurone is classified as "not likely to be carcinogenic to humans" based on data showing no treatment related increase in tumor incidence in rat and mouse carcinogenicity studies.		

FQPA SF = Food Quality Protection Act Safety Factor. LOAEL = lowest-observed-adverse-effect-level. LOC = level of concern. mg/kg/day = milligram/kilogram/day. NOAEL = no-observed-adverse-effect-level. PAD = population adjusted dose (a = acute, c = chronic). RfD = reference dose. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies).

The evaluation of the chronic toxicity studies indicates that flupyradifurone is not carcinogenic. EPA has not made a common mechanism of toxicity finding for flupyradifurone and any other substances. This means that the available information support the conclusion that flupyradifurone does not have a common mechanism of toxicity with other substances.

Given the low likelihood of adverse effects on humans, more refined estimates of acute and chronic dietary risk were not necessary for flupyradifurone. The assessments incorporated the highest level residues on the commodities and default or empirical processing factors and conservative drinking water estimates of exposure. The dietary assessment also conservatively assumed that 100% of every crop was treated. Neither the acute nor the chronic dietary exposure and risk estimates exceed the Agency's level of concern (LOC).

Risk estimates based on short- and intermediate-term occupational (worker/applicator) exposure to flupyradifurone for both handler (mixing, loading, and application via the dermal and inhalation routes) and post-application activities (via the dermal route) were also below the Agency's LOC.

The "Sivanto™ 200 SL" formulation falls in the lowest acute toxicity categories of III (oral and dermal) and IV (inhalation). Thus, the labeling precautionary signal word is "CAUTION."

2. Assessment of Ecological Risk

The battery of tests required to assess the environmental fate and ecological effects of flupyradifurone is complete.

Flupyradifurone is nonvolatile and does not bioaccumulate. Although it is characterized as being persistent to very persistent (half-lives ranging between 38 to 400 days) and is moderately mobile to mobile, variable half-lives in soil indicate that its persistence and mobility depend on soil types and climatic conditions. The primary route of degradation is through aqueous photolysis (half-life = 2.5 days), and the major routes of dissipation include runoff, erosion, and leaching. Twelve field studies conducted in both North America and Europe indicate that flupyradifurone has biphasic degradation, *i.e.*, a period of rapid loss of roughly 78% of the residues followed by a slow decline of the remaining residues; however, the majority (83%) of the field studies resulted in dissipation half-lives of less than 3 months.

Similar to the human health risk assessment, estimates of risk for non-target plants and animals were generally low, based on conservative screening level exposure values and did not warrant further refinements. The risk assessment for aquatic organisms concluded the following:

- Flupyradifurone is slightly to practically non-toxic to aquatic vertebrates (fish and aquatic-phase amphibians) on an acute exposure basis, and risk estimates were below LOCs for these animals.
- Estimates of chronic risk did not exceed the Agency's LOC for fish and aquatic-phase amphibians.
- There are no risks of concern for aquatic plants.

- Although flupyradifurone is highly toxic to benthic invertebrates and marine crustaceans (mysid shrimp) on an acute exposure basis and acute/chronic risk estimates based on these data do not exceed LOCs, the compound is only slightly toxic to freshwater invertebrates that occupy the water column and to shellfish.

For terrestrial organisms, the risk assessment concluded:

- Only the proposed soybean seed treatment use resulted in chronic risk to birds (and to terrestrial-phase amphibians and reptiles for which birds serve as surrogates).
- Only the risk estimates for foliar uses of flupyradifurone exceeded the chronic risk LOC for terrestrial invertebrates based on laboratory studies; however, field-based studies did not indicate any long-term effects on these organisms.
- There are no risks of concern for terrestrial plants.
- The conservative screening-level risk assessment identified potential risk to mammals based on chronic dietary exposure assuming that the animal is feeding on the treated site continuously and that 100% of their diet contains flupyradifurone residues based on flupyradifurone applications from two or more crop cycles.

EPA is aware of public concerns regarding the potential effects that systemic pesticides may have on honeybees and insect pollinators in general. The Agency is also aware of public concerns regarding the neonicotinoid insecticides (Subgroup 4B) of the IRAC Group 4 insecticides. Although it is not a neonicotinoid, as an insecticide, flupyradifurone is unusual in that laboratory-based studies indicate that the compound is practically non-toxic to adult bees on an acute contact exposure basis. EPA also has data on flupyradifurone which is consistent with the Pollinator Risk Assessment Guidance adopted by EPA and PMRA. (http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance) The guidance has been widely reviewed and EPA is requiring such data for older pesticides in its Registration Review activities. Applying this guidance provided EPA with a robust set of studies assessment factors with which to evaluate potential risks to honey bees. For this evaluation EPA received data on the potential impacts of flupyradifurone on developing bees (larvae, pupae) and data which examined potential adverse effects on honey bee colonies. The registrant for flupyradifurone voluntarily (proactively) conducted such studies to inform this registration decision and submitted them to EPA with the original registration action.

These data underscore how flupyradifurone differs in its acute toxicity from other acetylcholine esterase inhibitors within the IRAC Group 4 as well as those in Group 1. While the acute oral toxicity study indicates that flupyradifurone is highly toxic to individual adult honeybees, longer-term laboratory-based studies of both larval and adult bees show no adverse effects up to the highest dietary concentration tested (*i.e.*, 10,000 micrograms per liter; 10,000 µg/L).

Studies of whole colonies, both under confined semi-field (tunnels) and full-field conditions, examined pollinator-attractive crops, under a conservative exposure scenario. The chemical had been consecutively applied to the site, first as a soil treatment, then as a seed treatment, then again as a foliar treatment at early bloom, and finally again as a foliar treatment at full bloom at the maximum application rate while bees were actively foraging. EPA's review found that flupyradifurone did not result in any adverse effect on overall colony performance or overwintering capacity relative to untreated colonies. Residues measured in pollen and nectar from treated plants indicated that flupyradifurone was typically higher in pollen than in nectar

and that in general, residues declined in pollen and nectar within a two-week window following treatment. Although these field studies indicated a transient increase in adult bee mortality and foraging activity within 24 hours of treatment, the effects were not statistically significant and did not have a measurable impact on the whole colony. In a study where bees were fed a flupyradifurone-spiked sugar solution for six consecutive weeks, there were no adverse effects detected in the treated honeybee colonies relative to untreated colonies. EPA considers the 38 studies used to characterize the potential exposure to and effects of flupyradifurone on bees to be comprehensive and compelling evidence that the compound is not having a pronounced effect on bees even though applications were made during full bloom while bees were actively foraging.

Alternatives

Flupyradifurone is expected to be an alternative insecticide to certain pyrethroids (bifenthrin, *zeta*-cypermethrin), neonicotinoids (thiamethoxam, imidacloprid, acetamiprid), organophosphates (chlorpyrifos, acephate) and avermectins (abamectin). From a human health standpoint, pyrethroids and neonicotinoids generally have somewhat longer re-entry intervals (REIs) for workers than flupyradifurone which has a 4-hour REI. Additionally, some individual chemicals in the pyrethroid and neonicotinoid classes require more personal protective equipment (PPE) for handlers than does flupyradifurone. Organophosphates (OPs) and abamectin are more acutely toxic to humans than flupyradifurone and have varying degrees of REIs and PPE. Some uses involving OP pesticides have been subject to mitigation, owing to risk concerns. Thus, the risk to human health from flupyradifurone compares favorably to these alternatives.

As is typical with most insecticides, flupyradifurone may pose a risk to aquatic invertebrates; however, it is evident that flupyradifurone is less toxic than the majority of the alternatives. For example, comparing the freshwater invertebrate LC_{50} values for *zeta*-cypermethrin (0.0036 µg a.i./L), chlorpyrifos (0.06 µg a.i./L) and abamectin (0.34 µg a.i./L) shows they are much more toxic than flupyradifurone with an LC_{50} of 63.9 µg a.i./L. The estuarine/marine invertebrate LC_{50} value is 0.0035 µg a.i./L for chlorpyrifos, 0.004 µg a.i./L for bifenthrin and 0.02 µg a.i./L for abamectin versus 250 µg a.i./L for flupyradifurone. The cyano-substituted neonicotinoid acetamiprid is three times as toxic as flupyradifurone to freshwater invertebrates, and the nitroguanidine-substituted neonicotinoid thiamethoxam is approximately twice as toxic.

EPA determined that on a comparative hazard basis, flupyradifurone is less toxic to mammals on a chronic exposure basis than most of the leading market alternatives. In a comparison of chronic "no adverse effects level" and "no adverse effects concentration" values, flupyradifurone is much less toxic than abamectin, chlorpyrifos, fenpropathrin, bifenthrin, acephate and *zeta*-cypermethrin.

In terms of risk to birds, the avian LD_{50} value for flupyradifurone is 232 mg a.i./kg body weight showing that it is much less toxic than chlorpyrifos (LD_{50} = 5.62 mg a.i./kg), acetamiprid (5.68 mg a.i./kg), abamectin (85 mg a.i./kg), acephate (109 mg a.i./kg) and imidacloprid (152 mg a.i./kg).

As noted above in section 2 of the Evaluation (Assessment of Ecological Risk), flupyradifurone is classified as practically non-toxic to honeybees on an acute contact exposure basis. Table 2 compares the acute toxicity (96-hr LC_{50}) values of flupyradifurone to the registered alternatives and relative to the alternatives with respect to acute toxicity to honey bees, flupyradifurone is the least toxic.

Table 2. Honeybee acute 96-hr contact LC_{50} values

Chemical	LC_{50} µg a.i./bee
Bifenthrin	0.015
Zeta-cypermethrin	0.023
Thiamethoxam	0.024
Spinetoram	0.024
Chlorpyrifos	0.059
Imidacloprid	0.078
Abamectin	0.54
Acephate	1.2
Acetamiprid	<12.5
Flupyradifurone	**122**
Pyriproxyfen	>100
Spirotetramat	>100

Benefits

Flupyradifurone was submitted to the EPA's Office of Pesticide Programs (OPP) as a Reduced Risk compound for the proposed uses. Based on OPP's Reduced Risk Committee's evaluation, and as noted above in the Alternatives section, the human health and ecological hazard profiles for flupyradifurone are very favorable compared to currently registered alternatives.

Although there are a number of insecticides that interact as either inhibitors or modulators of the acetylcholine esterase enzymes involved in the transmission of nerve impulses and even among those that specifically inhibit the nicotinic acetylcholine esterase (IRAC Group 4), flupyradifurone is in a subgroup of its own (*i.e.*, the butenolides) due to distinct differences in how it interacts with the acetylcholine esterase receptor and how the chemical is metabolized. The differences between flupyradifurone and other chemicals within Group 4 (*e.g.*, neonicotinoids) make the new insecticide an effective means of reducing the likelihood of target pests developing resistance.

Flupyradifurone demonstrates efficacy against a variety of piercing, sucking insects, including species that are challenging to control (*e.g.*, scales, whiteflies), transmit disease (Asian citrus psyllid, Potato psyllid) and/or are known to rapidly develop resistance (whiteflies). It targets specific pests that growers have reported are causing serious damage to crops resulting in significant economic losses. In some locations, the registered alternatives, including neonicotinoids are failing to provide sufficient control for resistant pests. The pests identified by

the commenters include the Blue Alfalfa Aphid, Grape mealybug and vine mealybug, cotton aphid and whiteflies. Currently, there are no registered products that are adequately efficacious against the sugarcane aphid; however, field trials have indicated that flupyradifurone is very effective against this pest. Growers of prickly pear cactus face multiple pest challenges but have few registered products that are effective. Data from the USDA National Institute of Food and Agriculture funded Interregional Research Project Number 4 (IR 4) specialty crop and pest management program has supported the inclusion of this crop on the flupyradifurone label. Thus, registration of flupyradifurone will provide many growers of very diverse crops across the U.S. with a new pest management tool that presents an effective countermeasure to resistance development.

Public Comments

On May 29, 2013, EPA published a Notice of Receipt in the Federal Register of an application for registration of flupyradifurone and announced a public comment period of 30 days. Two comments were received.

The first comment expressed concern that neonicotinoid chemicals and other toxic substances are poisoning the environment, specifically citing concerns over cancer (generally) and concerns regarding pollinator exposure to toxic substances. This comment was not specifically addressing the application to register flupyradifurone but generally directed at the registration of pesticides in general.

In response to this comment, the EPA reiterates that flupyradifurone is not classified as a carcinogen. Also, as an insecticide flupyradifurone is unusual in that it is classified as practically non-toxic to honeybees on an acute contact exposure basis. While the compound is highly toxic to adult worker bees and can result in a transient increase in forager bee mortality, multiple semi-field and full-field studies did not indicate any significant adverse effect on honeybee colony performance and/or overwintering capability. Therefore, relative to many of the available registered alternatives, EPA considers the likelihood of adverse effects (risk) as a result of exposure from the proposed uses of flupyradifurone to be low.

The second comment was from The City of Sacramento Department of Utilities. They expressed concern that registering the chemical flupyradifurone for use on rice will affect drinking water quality in Sacramento. In regard to this second comment, the applicant did not apply for a use on rice.

On June 5, 2013, the EPA published a Notice of Filing in the Federal Register announcing the receipt of the initial filing of the flupyradifurone petition by Bayer Crop Science under the Federal Food, Drug and Cosmetic Act (FFDCA) requesting the establishment of regulations for residues of flupyradifurone on various commodities. This publication also announced a public comment period of 30 days; no comments were received on the FFDCA Notice of Filing.

The EPA announced the proposed decision of the unconditional registration for flupyradifurone on September 25, 2014, and held a public comment period for 30 days, closing October 25, 2014

at 11:59 pm. Twenty-five comments were received during the public comment period, two comments were duplicative; therefore there are twenty-three distinct individual comments posted to the docket. EPA's review and responses are summarized in a separate response to public comments document and is available in the Docket (Docket ID: EPA-HQ-OPP-2013-0226).

Twenty-one comments submitted to the docket supported EPA's proposed decision to register flupyradifurone as a new insecticide active ingredient. There were two comments in opposition of EPA's proposed decision. Supporting comments were submitted by University Research and Extension agents, USDA's IR-4, grower and commodity organization groups representing potatoes, apples, citrus, hops, cotton, wine grapes, alfalfa and growers of hydroponic tomatoes and cucumbers. Individual growers also wrote in support of the registration.

Commenters supporting the registration identified complex pest problems where there are few tools available to combat destructive pests that affect crop production and vector disease. One such pest is the sugarcane aphid which is currently crippling sorghum production in Mississippi, Georgia, and Oklahoma. According to a range of stakeholders, this pest is spreading fast and has moved from sugarcane to sorghum relatively quickly. There are no registered alternatives available that are efficacious against the sugarcane aphid. Sorghum growers have already experienced significant losses and view this pest as the most devastating threat they have ever seen. Emergency exemptions for an unregistered compound (sulfoxaflor) were granted to eight states to combat sugarcane aphid, the only other alternative is high treatment levels of the organophosphate insecticide chlorpyrifos.

The citrus growers are also very eager to use flupyradifurone against the Asian citrus psyllid which transmits citrus greening disease. This disease has severely harmed the Florida citrus industry where fruit yields are significantly impacted. Over time, the citrus greening disease is capable of killing infected trees. It now threatens the California citrus industry. The distinct differences in the activity of flupyradifurone relative to other insecticides is expected to provide an effective countermeasure for growers in these critical situations. It will also fit well into Integrated Pest Management (IPM) programs to provide a rotational tool and alternative to current pest control strategies.

One commenter who opposes to the registration of flupyradifurone focused on potential harm to honey bees and expressed concern for their exposure to flupyradifurone in the water column. The commenter noted that flupyradifurone is very highly toxic to freshwater insects and also indicated that additional applications will cause adverse effects to honey bees. They cited possible risk from the persistence of the degradates. The commenter also was critical of the validity of the semi-field and feeding studies. The other commenter in opposition to the EPA's proposed decision to register flupyradifurone based their concern on EPA not consulting with the U.S. Fish and Wildlife Service and National Marine Fisheries Service under the Endangered Species Act on the registration of a new active ingredient that may affect protected species.

Regulatory Decision

The flupyradifurone database is comprised of 437 studies and is considered to be complete as well as robust. In cooperation with our regulatory partners in Australia and Canada, and

considering the assessed risk to human health and the environment, the Agency concludes that flupyradifurone meets the regulatory standard under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). There are no outstanding data requirements for flupyradifurone. Therefore, the EPA is granting the unconditional registration of flupyradifurone under Section 3(c)(5) of FIFRA.

The PMRA of Canada proposed the registration of flupyradifurone in September, 2014 followed by a 45 day comment period. Their proposal includes both the foliar product and the soybean seed treatment product; final registration and use in Canada is anticipated in early 2015. Authorization of flupyradifurone in Australia is anticipated in early 2015.

In the U.S., two products will be registered, the technical formulation "Flupyradifurone TC," and the end-use formulation "Sivanto™ 200 SL." Sivanto™ 200 SL may be applied as a foliar application, by chemigation, and by soil drench. The maximum annual application rate is 0.365 lb a.i./A/year. All of the proposed uses listed in the beginning of this document (see "Background") will be registered. EPA is still considering its position for the flupyradifurone soybean seed treatment product and is not ready to make a decision at this time on that particular use pattern. However, a use pattern involving foliar application on that crop is being registered now.

EPA is not granting uses that were proposed for the entire Crop Group 18 on a national basis, the non-grass animal feeds (forage fodder, straw and hay) group. Uses of flupyradifurone for non-grass animal feeds will only be granted for clover exclusively in Washington, Oregon, and Idaho, and for alfalfa nationally. An insufficient number of clover trials was submitted to support the tolerance for the entire crop group.

For the food uses, Canadian Maximum Residue Levels (MRLs) and U.S. tolerances are harmonized for primary crop commodities.

Although the risks to non-target organisms and to human health from the use of flupyradifurone are considered to be low, the following mitigation has been added to the label:

- For further protection of workers engaged in a high contact activity, the restricted entry interval for girdling and cane turning activities in grapes is 48 hours.
- For foliar applications, the number of crop cycles per year has been limited to one for all crops except Brassica (Cole) leafy vegetables and leafy vegetables.

The risk assessments supporting this decision can be found in the regulatory docket (Docket ID: EPA-HQ-OPP-2013-0226).